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Purpose/Objective: Radiation therapy (RT) after radical prostatectomy (RP) improves prognosis in patients with high risk prostate cancer. However 5-year biochemical recurrence-free survival (bRFS) is only 75-80%. An advantage of hypofractionation is to reduce RT duration and to improve the probability of cure. However hypofractionation is potentially associated with an increased incidence of late toxicity, especially after RP. Data on efficacy and tolerability of hypofractionated RT in the postoperative setting are still lacking. Therefore, aim of this study is to compare two different trials using postoperative RT with conventional fractionation versus hypofractionation.
Materials and Methods: In an observational study, postoperative RT was performed with three dimensional conformal radiotherapy (3DCRT) (Total dose: 70.2 Gy/1.8 Gy per fraction). In a fase I-II trial, postoperative RT was performed with intensity modulated radiotherapy (IMRT) using simultaneous integrated boost (SIB) technique (Total dose 62.5 Gy/2.5 Gy per fraction). In both trials, prophylactic nodal irradiation and/or adjuvant hormonotherapy were administered according to risk factors. bRFS (PSA < 0.2 ng/ml), local control, disease-free-survival (DFS) and overall survival (OS) were analyzed using Kaplan-Meier method. A comparison of the survival curves was performed using long rank test (univariate analysis) or Cox Proportional Hazards Method (multivariate analysis; covariates: risk group, nodal irradiation and hormonotherapy duration).
Results: Considering the two studies, 194 patients were enrolled. Three-year bRFS was 83.3% (pN0: 90.3% vs pN1: 62.5%). The results are shown in Table 1. In terms of bRFS there was no statistical difference between the two series, even at multivariate analisys (p= 0.689).

		Observational study 3D-CRT	fase I-II trial IMRT-SIB	p:
Number of patients		67	127	
Dose/fraction (Gy)		70.2/1.8	62.5 /2.5	
Risk groups according to NCCN-2014	low	1.5 %	0.8 %	
	intermediate	14.9 %	16.5 %	0.866
	high	83.6 %	82.7 %	
N1		20.6 %	6.8 %	**0.008**
R1		86.6 %	84.3 %	0.667
Acute toxicity	GI > G2 *	4.5 %	0.0 %	**0.019**
	GU > G2 *	1.5 %	0.8 %	0.665
Late toxicity free survival	GI > G1 §	83.9 %	97.7 %	**0.002**
	GU > G1 §	74.5 %	87.6 %	0.258
bRFS	(5 years)	85.2 %	80.1 %	0.689

*: RTOG scale ; §: RTOG-EORTC scale (% at 2 years); GI gastrointestinal; GU genitourinary;

Conclusions: High dose adjuvant RT modulated based on risk factors (+/- prophylactic nodal irradiation, +/- adjuvant hormonotherapy) produced a better biochemical control compared to standard postoperative RT. Patients treated with IMRT-SIB technique showed a lower rate of acute and late gastrointestinal toxicity.

PO-0739

Plasma citrulline is a potential biomarker for small bowel toxicity following radiotherapy for prostate cancer

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Purpose/Objective: Small bowel toxicity from external beam radiotherapy (EBRT) for prostate cancer is poorly predicted from current DVH based models. The dose absorbed by this mobile organ throughout a fractionated course of EBRT cannot easily be calculated from a single planning CT scan. Plasma levels of citrulline (an amino acid, secreted by the gut) is a putative biomarker of small bowel radiation induced damage and as such a decrease in levels may predict small bowel toxicity. In this prospective, clinical study, we explored the relationship between the change in plasma citrulline in relation to both gastrointestinal toxicity and small bowel dosimetry in patients receiving radical EBRT for prostate cancer.
Materials and Methods: We recruited 15 patients treated with EBRT to either prostate only (n=6) or prostate and pelvis (n=9). Plasma citrulline levels were measured prior to radiotherapy and weekly during treatment and at 6 weeks, 3 months and 6 months post EBRT. Bowel toxicity was assessed at the same time points using EPIC bowel summary scores. Small bowel dosimetry was calculated on a single pre-treatment radiotherapy planning scan.
Results: The strongest correlation between the fall in plasma citrulline levels from baseline and greatest bowel toxicity was observed after 3 weeks of radiotherapy (two tailed Spearman's rank test p=0.03). We further explored the ability of this week 3 plasma citrulline decrease to predict bowel toxicity up to one year post radiotherapy with two-tailed Spearman rank tests between radiotherapy week 3 citrulline change and EPIC bowel toxicity change. A strong predictive trend was noted with positive correlations at 6 weeks post radiotherapy (correlation co-efficient =0.594, p=0.025), 3 months post radiotherapy (correlation co-efficient =0.534, p=0.060), 6 months post radiotherapy (correlation co-efficient =0.606, p=0.037), 9 months post radiotherapy (correlation co-efficient =0.618, p=0.019) and 1 year post radiotherapy (correlation co-efficient =0.358, p=0.345). No significant correlation was found between changes in plasma citrulline levels or EPIC reported toxicity and the small bowel V15, dose to 1cm^3, dose to 17cm^3 or max point dose.
Conclusions: Decreases in plasma citrulline after 3 weeks of pelvic EBRT may have the potential to predict small bowel toxicity in prostate cancer patients receiving radical external beam radiotherapy. Further study in a larger cohort is warranted.

PO-0740

An image-guided SBRT phase II study with a dose of 42 Gy in 7 fractions for the localized prostate cancer

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Purpose/Objective: Hypofractionation for prostate cancer, and in particular SBRT, results in a means of radiobiological dose escalation and potentially represents a therapeutic gain and a more economical course of definitive radiation therapy.

We have performed a phase II study to evaluate the feasibility and acute toxicity of a stereotactic body radiotherapy (SBRT) with a dose of 42 Gy in 7 fractions in patients with localized prostate cancer at low/intermediate risk (according to NCCN score) and risk of lymph node involvement <17%.

Materials and Methods: Since 2012, 40 patients at low/intermediate risk for localized prostate cancer have been planned for SBRT [Table 1]. Fraction size is 6 Gy for 7 fractions scheduled to be delivered twice a week for a total dose of 42 Gy.

Treatment is been delivered with a VMAT technique, with 2 arcs using 6MV photons from a Varian 2300 iX linac, planned with Eclipse 10.0 TPS by the AAA algorithm carried out by 3 different planners. Dose prescription is the average dose to PTV with the request V95%≥ 95%.

The DVH constraints for OAR's have been derived from literature and local experience. To reduce the organ motion, patients has been premedicated before treatment with Butylscopolamine. The protocol is based on 3 IGRT intraprostatic fiducial markers, with daily online checks by CBCT. The acute and late toxicity has been recorded using the RTOG / EORTC scale and additional data has been collected by means of II-PSS (International Prostate Symptom Score) e IIEF-5 (International Index of Erectile Function) questionnaires.

Results: Thirty-two patients have been followed for three months or more while thirteen patients for 12 months or more. At 3 month, 12% of patients reported grades 1 urinary toxicities . At 6 months no patients reported grade 1 urinary toxicities. At 18 months, one patient each reported grade 1 proctitis and grade 1 rectal bleeding which resolved without intervention.

Biochemical response was rapid the first 12 months of follow up: mean pre-treatment and 12-month post-treatment values were 3,75 ng/ml and 0.7 ng/ml respectively.

By using pharmacological premedication of the patient we have a control of organ motion intrafraction (OMI) ≤ 2 mm in 98% of treatment sessions. The results of OMI movement are shown in Figure 1.

Conclusions: Intrafraction motion of the prostate is minimal when the patient follows the special diet and are premedicated before treatment with Butylscopolamine.

The proposed scheme is estimated more effective to high-dose conventional regimens. The absence of acute toxicity seems to confirm the validity of the adopted NTCP model and could be predictive of late toxicity.

At this early follow up point, prostate SBRT results in favorable toxicity and biochemical outcomes and appears to support the strategy of hypofractionation in the management of localized prostate cancer. Further follow up is necessary to validate these early, promising results.

PO-0741

Outcomes of conformal RT and ADT in high risk prostate cancer: is there a role for surgery?

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Purpose/Objective: Surgeons suggest an important role for radical prostatectomy in high risk pts. We reviewed outcomes and patterns of failure in high risk pts treated with conformal RT and androgen deprivation (ADT) to address the hypothesis that primary surgery offers additional benefit.

Materials and Methods: Pt records from 11/2001- 3/2012 were reviewed from an IRB approved database. High risk was defined as PSA ≥ 20 or Gleason score ≥ 8 or clinical stage ≥ T2c. Three treatment protocols were used: A. 2001-2009-3D conformal, B. 2004-2011 IMRT ± IGRT, C. 2011-2012 VMAT+IGRT. Groups A and B were treated using standard 2Gy/fx to 78-82 Gy. Group C was treated using hypo-fractionation with daily IGRT to 73.6Gy/2.3Gy, (dose =82Gy 2gy/eq., σ/ß=1.5). All pts received pelvic lymph node radiation therapy and 2 years of ADT (except 2 patients who declined ADT). Side effects were recorded using CTCAE version 4. Treatment failure was defined using the Phoenix definition (PSA> absolute nadir +2ng/ml). The Kaplan Meyer method was used to determine probability of survival and toxicity. P values ≤ .05 were considered significant.

Results: 203 patients were reviewed: Treatment group; A=30 pts, B=71 pts, C=102 pts. Median PSA: 15.1ng/ml (range: 1.4ng/ml – 449ng/ml). PSA< 50ng/ml=180 pts, PSA≥50ng/ml=23 pts. Gleason score: <7=15 pts, 7=46 pts, >7=142 pts. Clinical stage: <T2b=37pts, T2b=49pts, >T2b=117pts. Median follow up was 46 months (range: 12 - 142). Kaplan Meyer estimate of 4 year biochemical PSA free survival for all pts was 88%. Four year survival by subgroup was: treatment group: A=93%, B=90%, C=83%; PSA: PSA <=50ng/ml = 90%, PSA ≥ 50ng/ml = 64%; Gleason score: <7 = 100%, 7 =87%, >7 =88%; and stage: <T2b = 97%, T2b = 89% and >T2b 85%. Total treatment failures: (14%, 28/203pts). Treatment failure by subgroup: Treatment; Group: A (17%, 5/30 pts), B (15%, 11/71pts), C (12%, 12/102 pts) p=0.7; PSA: < 50 (11% , 20/180 pts), PSA ≥50 (35%, 8/23pts) p=0.03; Gleason score: <7 (7%, 1/15 pts), =7 (17%, 8/46pts), >7 (13%, 19/142pts) p=0.6; and Stage: <T2b (8%, 3/37pts), T2b (13%, 9/68pts), >T2b (16%, 16/98pts) p=0.5. Only PSA value was significant in uni- and multivariate analysis p=0.04. The median time to failure was 30m (range: 4m-76m). All failures were initially detected as biochemical recurrence only. Sites of recurrence: prostate 3pts, lymph nodes 3pts, bone 16pts, other 2pts, and biochemical failure 4pts. Two deaths are attributed to prostate cancer. Acute and late ≥grade 3 toxicity: Genitourinary: acute 6pts (3%), late 21pts (10%); Gastrointestinal: acute 2pts (1%), late 7pts (3.5%).

Conclusions: This contemporary series shows that high risk prostate cancer pts treated with conformal RT and ADT have favorable outcomes and experience low toxicity. PSA ≥50ng/ml is associated with worse outcomes. Distant failure was dominant and local recurrence in the prostate was rare, suggesting that primary surgery is unlikely to provide additional benefit.